Purpose: Despite improved staging and operative techniques, rate of incomplete resection (R1) of NSCLC has remained significant over the last decades. Patients with R1 resection have significantly worse survival compared to those with complete resection (R0). SBRT delivers high dose radiotherapy (RT) to tumours, in a short time (1-10 treatments), with high precision while sparing normal organs. The efficacy of SBRT in treating small lung tumours is documented but its use as neo-adjuvant therapy in LA-NSCLC is not reported yet. We hypothesized that a short course of pre-operative SBRT can be done safely and could improve rates of R0 resection of LA-NSCLC and conducted a Phase I trial (LINNEARRE I) to investigate the safety and feasibility of delivering, timely, neo-adjuvant SBRT in operable patients with LA-NSCLC at risk for positive resection margins.
Methods and Materials: Twenty appropriately staged (PET-CT/MRI and mediastinal staging) patients with biopsy proven T3-T4, N0-1, M0 NSCLC will be enrolled. Patients would be deemed medically operable by the surgical team but at risk of < R0 resection (due to invasion of mediastinal or hilar structures, chest wall or vertebral bodies). Primary outcome is feasibility i.e. the ability to complete SBRT as planned and proceed to surgery (Sx) within six weeks. Secondary outcomes include acute and late adverse events, R0/R1/R2 rates and secondary surrogates of feasibility. SBRT is delivered in over two weeks (in 10 fractions). Dose is escalated from 35 Gy to 50 Gy. Five patients will be accrued to each dose level of 35, 40, 45 and 50 Gy. At the latter dose level, normal tissue (nt) BED (133 Gy) exceeds that delivered concurrently with chemotherapy with 63-66 Gy/30 fractions (107-110 Gy) but is similar to that delivered by recent dose-escalation chemo-RT (74 Gy) studies. Clinical target volume (CTV) includes only the area of tumour deemed at risk of incomplete resection expanded by 3-5 mm into surrounding tissues where there is clinical suspicion of invasion.
Results: This study opened to accrual in late 2015. Dosimetric feasibility was tested in virtual plans of selected eligible cases that were planned to receive treatment at the highest planned dose level (50 Gy). All cases met dosimetric constraints for planned target volume (PTV) and organs at risk (OAR: great vessels, heart, esophagus, and proximal bronchi). Examples of virtual plans will be illustrated.
Conclusions: This is the first study to investigate SBRT as a neo-adjuvant therapy in LA-NSCLC. Virtual plans suggest that is feasible to deliver neoadjuvant SBRT safely to tumour volumes at risk for positive margins. A key aims of this study is to examine the adaptation of workflow in a Canadian academic institution to achieve timely neoadjuvant SBRT delivery. If successful this Phase I study will lead to further evaluation of pre-operative SBRT in LA-NSCLC, to help achieve improved rates of complete resection and improved outcomes.

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LIMITING CHEST WALL TOXICITY BY ADAPTING THE DOSE SCHEDULE AND DOSE CONSTRAINTS IN SBRT FOR EARLY-STAGE LUNG CANCER
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Purpose: Chest wall (CW) toxicity (rib fracture and/or pain) is a well-known complication after stereotactic body radiotherapy (SBRT) for early-stage lung cancer. The aim of this study is to evaluate the frequency of CW toxicity following SBRT and to determine the dosimetric parameters that influence the risk of CW toxicity.
Methods and Materials: We reviewed medical charts and radiotherapy (RT) plans from patients treated for T1 or T2N0 peripheral primary lung cancer between 2009 and 2015. Treatment was delivered by Cyberknife®, helical tomotherapy or using volumetric modulated arc therapy. CW structure corresponded to a 3 cm expansion of the lung excluding the lung volume. The median total dose delivered to the planning target volume was 60 Gy (range, 54- 60). SBRT was delivered in 3 fractions for patients with a CW V30 of less than 30cc. If the CW V30 exceeded 30cc, 5 fractions were delivered and the SBRT plan was optimized on the biologically equivalent parameter of CW V30: CW V37 < 30 cc. We studied the association between CW toxicity and delivered dose using the Student T-test.
Results: Three hundred and eighty-one lesions were treated in a cohort of 363 patients with a median follow up of 17 months (range, 1 - 62). Twenty patients (6 %) had CW toxicity: 13 patients (4%) developed CW pain and nine patients (3%) developed rib fractures. For patient treated in 3 fractions, the mean CW V30 was 21 cc for patients with CW toxicity and 16 cc for patients without toxicity ($p < 0.05$). For patients treated in 5 fractions (n = 55), the small number of patients with chest wall toxicity did not allow comparison of V37 between groups. The CW V37 was inferior to 30 cc for all patients. CW toxicity rates were similar in the 3 or 5 fractions group (6% versus 4%). The two-year local control was similar in the two groups (96% versus 94%).
Conclusions: This study confirms that CW V30 is significantly associated with CW toxicity. When the CW V30 is greater than 30 cc, delivering SBRT in 5 fractions and with a CW V37 of less than 30 cc can limit CW toxicity without compromising tumour control.

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IS IT TIME FOR ADJUVANT CHEMOTHERAPY AFTER SBRT OF EARLY-STAGE NON-SMALL CELL LUNG CANCER?
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Purpose: Surgery remains the standard treatment for medically operable patients with early-stage non-small cell lung carcinoma (NSCLC). Adjuvant chemotherapy is routinely recommended following resection of tumours > 4 cm. For patients who decline surgery or are medically unfit, stereotactic body radiation therapy (SBRT) has emerged as an excellent alternative. The benefit of adjuvant chemotherapy following lung SBRT has not been studied. To evaluate the potential benefit of such a treatment, we reviewed the outcomes of T2N0 patients treated with SBRT.
Methods and Materials: We reviewed patients treated with SBRT for primary early-stage NSCLC between 2009 and 2015. Total target doses were between 50 and 60 Gy, administered in 3 – 8 fractions. All patients had a staging FDG PET/CT and histologic confirmation was obtained whenever possible (70 %). Mediastinal staging (MS) was performed if lymph node involvement was suspected on CT or PET/CT. Survival outcomes were estimated using the Kaplan-Meier method.
Results: Among the 556 NSCLC early stage patients treated with SBRT, 115 patients were staged T2N0. In T2N0 patients, the mean lesion size was 3.4 cm (range, 3 - 4.6cm). The one-year and three-year overall survival were 88% and 68% for patients with T2 disease, compare to 95% and 80% for the T1N0 patients ($p < 0.05$). The median disease-free survival was higher in the T1N0 group (48 versus 32 months). For T2N0 patients, the one-year and three-year local control rates were 98% and 91% respectively. Twenty patients (16.5%) presented a relapse, amongst which 16 (80%) were nodal or distant. The median survival of T2N0 patient post-relapse was 20 months.
Conclusions: Lung SBRT provided high local control rates, even for larger tumours. Overall survival and patterns of failure are similar to surgery. It remains to be seen if SBRT patients will be fit for and accepting of adjuvant chemotherapy but these results raise the question if adjuvant treatment is advisable post SBRT.

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DOES EARLY TUMOUR REGRESSION OBSERVED ON CONE-BEAM COMPUTED TOMOGRAPHY DURING CHEMO-RADIOTHERAPY PREDICT FAVOURABLE OUTCOME IN LOCALLY ADVANCED LUNG ADENOCARCINOMA?
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Purpose: Tumour volumetric changes can be observed during radical chemo-radiotherapy (CRT) for locally advanced non-small cell lung cancer (NSCLC); but it is unclear whether these changes are predictive of outcomes. This study aims to a) examine whether the magnitude of tumour regression is correlated with disease control and survival; b) explore the potential difference between adenocarcinoma (AC) and non-adenocarcinoma (non-AC) NSCLC subtypes.
Methods and Materials: Primary tumour volumes were recorded and analyzed on weekly serial cone beam computed tomography (CBCT) images of NSCLC patients treated with CRT from January 2006 to June 2007 at our institution[1]. Tumour volume regression was divided into three categories: < 10%, 10-30%, and ≥ 30%. Outcome measures included locoregional failure-free survival (LRFFS), distant failure-free survival (DFFS), and overall survival (OS), which were calculated using the Kaplan-Meier method. Univariate analysis (UVA) and multivariate analysis (MVA) of LRFFS, DFFS and OS were performed using the Cox regression model. Further analysis was performed comparing AC and non-AC subgroups.
Results: Forty-five patients with Stage II-III NSCLC were included. Median age was 64 years (range: 43 – 79 years). Median follow up was 22.1 months for all patients, and 90 months for alive patients (range: 0.9-108 months). The distribution of 7th Ed. AJCC stage was as follows: Stage IIB (T3N0) 8.9%; IIIA 66.7%; IIIB 24.4%. Twenty patients (44.4%) had AC, while 25 patients (55.6%) had non-AC histologies. All patients received concurrent chemotherapy. Twenty-eight patients (62.3%) received a total radiation dose of ≥ 60 Gy, 15 patients (33.3%) received 45 Gy as part of trimodality therapy determined upfront, and two patients (4.4%) received 58-59 Gy due to missed fractions. Among all 45 patients, 23 patients (51.1%) had ≥ 30% regression by fraction 15 and 32 patients (71.1%) by treatment completion. In UVA for all patients, young age (p = 0.02) and AC histology (p = 0.03) were significantly associated with better LRFFS; young age was significantly associated with better DFFS (p = 0.048) and OS (p = 0.04). For patients with AC histology, MVA showed that ≥ 30% regression by fraction 15 and younger age were significantly associated with better LRFFS (p = 0.007, 0.006 respectively), DFFS (p = 0.007, 0.004), and OS (p = 0.02, 0.004). For patients with non-AC histology, ≥30% regression by treatment completion was significantly associated with better LRFFS (p = 0.02), but none of the factors had any significant correlation with DFFS or OS.
Conclusions: Evaluation of primary tumour regression on CBCT images during CRT may be predictive of treatment response. Early tumour regression, as indicated by ≥30% regression by fraction 15, was shown to be associated with better outcomes for adenocarcinoma histologic subtype in our study. This observation may provide insight into when, how and in which patients to best utilize adaptive radiotherapy.
1. J Thorac Oncol. 2011; 6: 531-6.

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CUMULATIVE INCIDENCE OF BRAIN METASTASIS AFTER DIAGNOSIS OF NON-SMALL CELL LUNG CANCER: ESTIMATES FROM A REGIONAL CANCER CENTRE COHORT
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Purpose: Non-small cell lung cancer (NSCLC) is the most common primary cancer to metastasize to the brain. However, the incidence or likelihood of developing brain metastasis, after initial diagnosis and treatment, is generally unknown, as provincial population-based cancer registries do not routinely capture metastatic relapses. At our centre, a retrospective cohort study has gathered longitudinal clinical data for all NSCLC patients consulted since 1999 (Glans-Look Lung Cancer Database). In this report, we describe the cumulative incidence of brain metastasis observed for NSCLC patients diagnosed between 1999 and 2010.
Methods and Materials: Clinical data, including date of brain metastasis diagnosed by CT/MR imaging, is abstracted from electronic and paper charts by full time research coordinators. De novo cases of brain metastasis were defined as positive CT/MR within 30 days of initial cancer diagnosis and distinguished from relapsing cases (Stages I-IV at initial diagnosis). Cumulative incidence of relapsing brain metastasis was computed, stratified by cancer stage at initial diagnosis and adjusted for competing risk of death before developing brain metastasis. Survival difference between de novo and relapsing brain metastasis (those initially Stage I-III) was examined by pre-specified proportional hazard regression model, adjusting for age and year of diagnosis.
Results: A total of 5,264 NSCLC incident cases diagnosed between 1999 and 2010 were identified and analyzed (90% have died). Median age at initial cancer diagnosis was 70 years. Proportion of Stage I, II, III and IV patients was 18%, 8.3%, 20% and 54% respectively. A total of 451 patients relapsed with brain metastasis, giving a five-year cumulative incidence of 8.6%, 14% and 8.0% for Stage I-II, Stage III, and Stage IV, respectively. Among the 2,827 Stage IV patients, 631 (22%) and 179 (6.3%) had de novo and relapsing brain metastasis, respectively. Median survival of de novo brain metastasis (n = 631, 3.2 months, CL 2.8-3.5 months) was worse than that for Stage I-III relapsing cases (n = 272, 3.9 months, CL 3.3-4.7 months), adjusted HR 1.24, CL 1.07-1.44 months.
Conclusions: The five-year cumulative incidence of brain metastasis was 8.6%, 13%, and 8.0% among Stage I-II, Stage III and Stage IV NSCLC patients. Twenty-two percent of Stage IV NSCLC patients presented with de novo brain metastasis, whose median survival was significantly worse than that for Stage I-III patients with relapsing brain metastasis.

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RADIOTHERAPY FOR PALLIATION IN KAPOSI SARCOMA
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Purpose: Kaposi sarcoma (KS) is a non-curable malignancy which can present with cutaneous lesions. Some patients with KS can have a long indolent chronic course. Radiotherapy is often used to help palliate local symptoms for cutaneous lesions which bleed or cause pain.
Methods and Materials: A retrospective review was undertaken for all KS patients treated with radiotherapy at our centre from January 2, 1999 to December 31, 2014 (inclusive). This study was approved by the local hospital Research Ethics Board. Demographic information (date of birth, gender, co-morbidities) were retrieved along with radiotherapy details, symptoms, treatment side-effects and outcomes.
Results: A total of 48 patients with KS (44 classical, 0 endemic, one iatrogenic, three AIDS related) were seen in our multidisciplinary skin clinic during this study period. Eighteen patients received radiotherapy to 107 sites (1-20 sites per patient). There were five females and 13 males. Ages at the time of initial radiotherapy ranged from 44-93 years of age. Radiotherapy dose ranged from 6 Gy in 1 fraction to 30 Gy in 10 fractions with the most common scheme being 8 Gy in 1 fraction or 20 Gy in 5 fractions. Of the 107 sites treated, 106 showed regression of the KS lesions with benefit in terms of pain, swelling or bleeding. One site in the posterior leg showed progressive KS despite 8 Gy in 1 fraction which continued to bleed and ulcerate. Two patients had initial partial response to radiotherapy but had relapse within the radiated fields requiring repeat radiotherapy. One patient had relapse within the radiated fields and subsequently was observed. No fatal toxicities occurred. The most common side effects were dry desquamation, hyperpigmentation and lymphedema of the legs.